Les microparticules (MP) sont des fragments de membrane désormais reconnus comme marqueurs fiables de l'activation et de l'apoptose cellulaires.

Objectif — Notre objectif a été de déterminer si les taux de MP issues de différents types cellulaires étaient associés à la sévérité des lésions athéromateuses et à la récurrence d'événements cardiovasculaires chez des patients coronariens.

Méthodes et Résultats — Les taux plasmatiques de MP ont été mesurés par cytométrie en flux chez 172 patients en attente de coronarographie à l'hôpital de la Timone. 77 patients (46%) ont bénéficié d'une pose de stent et ont été suivis durant 1 mois. 12 événements récurrents ont été rapportés pendant la période de suivi. Dans la cohorte totale, les taux de MP positives pour le marqueur d'activation leucocytaire CD11b (MPCD11b+) étaient significativement plus élevés chez les patients traités par des statines ($p = 0,001$) et chez les patients ayant une fraction d'éjection préservée ($p = 0,02$). Les taux de MPCD11b+ étaient significativement mais négativement associés à l'étendue des lésions athéromateuses coronaires évaluée par les données angiographiques et par le Syntax Score, ceci même après ajustement sur le traitement par les statines et sur la fraction d'éjection ($p = 0,005$). Au sein de la population stentée, les taux de MPCD11b+ étaient significativement inférieurs chez les patients ayant présenté un événement récurrent ($p = 0,0001$). Cette différence restait significative après ajustement sur le Syntax Score, sur la fraction d'éjection et sur le traitement par des statines ($p = 0,03$).

Conclusion — Les MPCD11b+ sont un marqueur biologique qui permet d'identifier les patients coronariens à haut risque de récurrence indépendamment de la sévérité des lésions observées lors de la coronarographie.

E005

MICROPARTICLES FROM T LYMPHOCYTES REDUCE ACTINOMYCIN-D INDUCED APOPTOSIS IN HUMAN ENDOTHELIAL CELLS

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Recent studies have demonstrated that microparticles (MPs) generated from T lymphocytes undergoing both activation and apoptosis correct endothelial injury, and regulate angiogenesis. These effects are mediated by an increase of NO release and a decrease of reactive oxygen species (ROS) production. Apoptosis is an important mechanism that controls endothelial cell number and regeneration. We studied the effects of these MPs on human umbilical vein endothelial cell (HUVEC) apoptosis induced by actinomycin D (actD). Engineered MPs were obtained by activation of human lymphocyte CEM-T cell line with phytohemagglutinin and then, by stimulation with phorbol-12-myristate-13-acetate and actD. HUVECs were grown for 24h in absence or presence of the proapoptotic agent actD (1 µg/ml), and/or 10 µg protein/ml of MPs. In another set of experiments, endothelial cells were pre-incubated either with nonselective caspases inhibitor, z-vad.fmk (50 µm), PI3-kinase inhibitor, LY294002 (10 µm), ERK inhibitor, U0126 (10 µm), NOS inhibitor, L-NA (100 µm), or the superoxide dismutase (SOD) mimetic, manganese(III)tetrakis-(1-methyl-4-pyridyl)-porphyrin pentachloride (MnTMPyP, 100 µm). The proportion of nuclei with hypodiploid DNA (sub-G1 peak) corresponding to apoptotic cells was determined by flow cytometry after staining with propidium iodide, and by microscopy using TUNEL labeling. Our results clearly indicate that activated/apoptotic T lymphocytes MP treatment significantly reduces HUVEC apoptosis evoked by actD. Moreover, pancaspases inhibitor reduces the degree of cell death either in presence or in absence of MPs, indicating the implication of caspases in actD-induced apoptosis. Although, the PI3-kinase inhibitor induces apoptosis by itself, it does not blunt the capacity of MPs in reducing apoptosis induced by actD. In contrast, the inhibitory effect of MPs is prevented in the presence either of the ERK inhibitor or the NOS inhibitor. Interestingly, MnTMPyP reduces actD-evoked apoptosis and the protective effects of MPs. Thus, these MPs may act as an SOD mimetic under these experimental conditions. Altogether, T lymphocyte MPs evoked cell protection against apoptosis at the level of caspases inhibition, MAP kinases, NO and ROS formations. They underscore the potential therapeutic of such MPs against vascular pathologies in close association with apoptosis.

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E006

INFLUENCE OF MICROPARTICLES HARVESTED FROM PATIENTS AFFECTED BY OBSTRUCTIVE SLEEP APNEA SYNDROME ON ENDOTHELIAL FUNCTION AND VASCULAR REACTIVITY

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Obstructive sleep apnea syndrome (OSAS) is a highly prevalent disease characterized by recurrent episodes of partial or complete obstruction of the upper airways during sleep, leading to oxygen desaturation, sleep fragmentation and clinical endothelial dysfunction. Microparticles (MPs) are membrane vesicles released during cell activation and apoptosis. Elevated levels of circulating MPs have been detected in pathologies associated with vascular alterations. We investigated the effects of MPs on endothelial function and vascular reactivity in OSAS. Blood samples were obtained either from 38 OSAS patients without any other cardiovascular comorbidities and 23 healthy subjects. A desaturation index above 10 per hour defined OSAS patients. MPs concentration and origin were assessed using flow cytometer. Male Swiss mice were injected i.v. with MPs from OSAS or healthy subjects, or with saline solution, and sacrified after 24 hours. Endothelial function and vascular reactivity were studied on aortic rings and small mesenteric resistance (SMA) arteries by myography and arteriography, respectively. Patients with OSAS did not display increased circulating levels of MPs compared to healthy subjects including those from pro-coagulant, platelet, endothelial, leukocyte and erythrocyte origins. Interestingly, MPs from granulocytes and activated leukocytes were significantly enhanced in OSAS patients. Activated leukocyte MPs positively correlated with oxygen desaturation index. In aorta, MPs from OSAS patients but not those from healthy subjects significantly reduced endothelium-dependent relaxation to acetylcholine. MPs from OSAS increased sensitivity of the aorta in response to serotonin that was greater compared to the effect of MPs from healthy subjects. In SMA, MPs from OSAS but not those from healthy subjects impaired flow-induced dilation without any effect on myogenic tone. Although SMA from mice